REVIEW ON DIFFERENT METHODS OF SYNTHESIS OF 2-AMINO SUBSTITUTED BENZOTHIAZOLE

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ABSTRACT
2-Amino – Benzothiazole and its derivative has attracted strong interest due to their pharmacological properties. Benzothiazole nucleus contain various biological activities like Anti-microbial, Anti-convulsant, Anti-tumor, Anti-cancer, Anti-inflammatory, etc. This review paper is focused on various different methods of synthesis of 2-amino substituted Benzothiazole because of wide biological activities.

KEYWORDS: Substituted Benzothiazole, Biological Activities.

INTRODUCTION
Benzothiazole is a heterocyclic compound, weak base, having varied biological activities. Benzothiazole moites are part of compounds showing numerous biological activities such as anti-cancer, anti-microbial, anthelmintic, antidiabetic, activities. Benzothiazole are bicyclic ring system with multiple application attracted attention to review.

SYNTHESIS
Various methods had been reported. Some methods were listed in this study.

Scheme -1
An efficient and convenient method was developed for synthesis of 2-benzothiazole through copper catalyzed condensation of 2-amino benzothioles with nitriles.

\[
\begin{align*}
\text{R} & \quad \text{NH}_2 \quad \text{SH} \\
+ & \quad \text{NC-}R' \\
\xrightarrow{0.1 \text{ eq. Cu(OAc)}_2, 1 \text{ eq. } \text{NEt}_3, \text{EtOH, 70°C, 6 h}} \\
\text{R} & \quad \text{NH} \quad \text{S} \quad \text{R'} \\
\end{align*}
\]

R: H, Cl
R': Ar, alkyl, benzyl
Scheme-2
A p-substituted aniline can be converted into 2-amino-6 substituted Benzothiazole by using sodium thiocyanate in presence of sulphuric acid.

\[
\text{Ar-H} + 3 \text{ eq. } \text{NH}_4\text{SCN} \xrightarrow{1.5 \text{ eq. } \text{Br-SMe}_2\text{Br}^-} \text{MeCN, r.t., 5-30 min} \rightarrow \text{Ar-SCN} \quad \text{Ar: activated aromatics}
\]

Scheme-3
A tandem approach enables a facile and efficient synthesis of various 2-aminobenzothiazoles from 2-chloroanilines and dithiocarbamates in excellent yields in the presence of Pd(PPh$_3$)$_4$ and t-BuOK.

\[
\text{R-NH}_2 + 3 \text{ eq. } \text{NH}_4\text{SCN} \xrightarrow{1.5 \text{ eq. } \text{Br-SMe}_2\text{Br}^-} \text{MeCN, r.t., 25-40 min} \rightarrow \text{R-SCN}
\]

Scheme-4
A wide range of 2-arylbenzothiazoles can be obtained in high yields by simply heating o-halonitrobenzenes, acetophenones, elemental sulfur, and N-methylmorpholine. This three-component coupling occurs in an excellent atom-, step-, and redox-efficient manner with elemental sulfur as nucleophile building block and redox moderating agent.

\[
\text{R-N}_{2} \xrightarrow{4 \text{ eq. } S} \text{R-SCN} \xrightarrow{2 \text{ eq. NMM}} \text{R-N}_{2}
\]

Scheme-5
In the presence of Cul and 1,10-phen, and n-P$\text{Pr}_3$N as the base, (2-iodobenzyl)triphenylphosphonium bromide and (2-iodophenylimino)triphenylphosphorane reacted efficiently with thiocarboxylic acids to give benzo[b]thiophenes and benzothiazoles in good yields via sequential Ullmann-type C-S bond coupling and subsequent Wittig reaction.

\[
\text{R-PPh}_3\text{Br} + 1.1 \text{ eq. } \text{O}_{\text{Ar}} \xrightarrow{5 \text{ mol-% Cul, } 0.1 \text{ eq. 1,10-Phen}} 2.5 \text{ eq. NPr}_3 \xrightarrow{\text{dioxane, 100°C, 32 h}} \text{R-N}_{2}
\]

\[
\text{R-N}_{2} + 1.1 \text{ eq. } \text{O}_{\text{Ar}} \xrightarrow{5 \text{ mol-% Cul, } 0.1 \text{ eq. 1,10-Phen}} 1.5 \text{ eq. NPr}_3 \xrightarrow{\text{dioxane, 100°C, 32 h}} \text{R-N}_{2}
\]
The use of Pd/C as catalyst enables a ligand-free and additive-free synthesis of 2-substituted benzothiazoles via cyclization of o-iodothiobenzanilide derivatives at room temperature. The protocol is high-yielding and involves very mild conditions.

Dess-Martin periodinane (DMP) efficiently mediates the intramolecular cyclization of phenolic azomethines at ambient temperature leading to substituted benzoazoles and benzothiazoles. Treatment of the reaction mixtures sequentially with Amberlyst A-26 thiosulfate resin and diisopropylaminomethyl resin (PS-DIEA) removes excess reagent and byproducts, to give pure products.

CONCLUSION
The reviewed new class of 2-substituted amino Benzothiazole has shown a wide spectrum of biological activities. The substituted benzothiazoles having anti cancer, anti diabetic, anti tumor and anti microbial activities. The biological profiles of these new generation of Benzothiazole represents much progress with regards to the older compounds.

REFERENCES